Exhibit 14

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

IN RE: '318 PATENT LITIGATION	**Civil Action No. 05-356 (KAJ)** **(Consolidated)**

DEFENDANTS BARR PHARMACEUTICALS, INC.'S AND BARR LABORATORIES INC.'S SUPPLEMENTAL OBJECTIONS AND RESPONSE TO PLAINTIFFS' INTERROGATORY NO. 2

Pursuant to Rules 26 and 33 of the Federal Rules of Civil Procedure, Defendants Barr Pharmaceuticals, Inc. and Barr Laboratories, Inc. (collectively "Barr") supplement their response to Plaintiffs' Interrogatory No. 2. Barr reserves the right to supplement or amend its objections and response as it obtains additional information during the course of discovery.

GENERAL OBJECTIONS

The following general objections to Plaintiffs' Interrogatories (including Definitions and Instructions) are hereby incorporated into Barr's supplemental objections and response to Plaintiffs' Interrogatory No. 2 as if fully set forth therein.

1. Barr objects to Plaintiffs' Interrogatories to the extent they call for responses that would require disclosure of information that is protected by the attorney-client privilege, the attorney work-product doctrine, or any other evidentiary privilege.

2. Barr objects to Plaintiffs' Interrogatories (including Definitions and Instructions) to the extent that they purport to impose discovery obligations beyond those required under the Federal Rules of Civil Procedure, the Local Rules of Civil Practice and Procedure of the United States District Court for the District of Delaware, and any applicable Orders of the Court or agreements between counsel. Barr will follow the governing rules, orders, and agreements in

responding to these Interrogatories. Barr particularly objects to the Definitions and Instructions on these grounds to the extent that they call for response obligations beyond those required by Federal Rule of Civil Procedure 26(b)(1).

3. Barr objects to Plaintiffs' Interrogatories to the extent they are overly broad, unduly burdensome, and/or not reasonably calculated to lead to the discovery of admissible evidence.

4. Barr objects to Plaintiffs' Interrogatories to the extent an Interrogatory, or any words or terms used therein, is vague, ambiguous, subject to different interpretations, requires subjective knowledge by any party other than Barr, or involves issues of law subject to resolution by the Court. Barr will answer to the extent possible based on the most objectively reasonable interpretation of the Interrogatory.

5. Barr objects to Plaintiffs' Interrogatories to the extent they seek information beyond the possession, custody, or control of Barr, or to the extent the information requested is as readily available to Plaintiffs (or more so) as it is available to Barr.

6. Barr objects to Plaintiffs' Interrogatories to the extent they seek confidential or proprietary information of a non-party or seek highly confidential business or technical information that is of little or no relevance to the claims or defenses in this action.

7. Barr objects to Plaintiffs' Interrogatories to the extent that they are premature and Barr reserves the right to supplement its response pursuant to Federal Rule of Civil Procedure 26(e).

8. Barr objects to Plaintiffs' Interrogatories, including the Definitions and Instructions, to the extent they purport to define words or phrases in a manner different than their ordinary use, and Barr's response to such Interrogatories shall not be construed as an admission, agreement, or acquiescence in such a definition.

9. Barr objects to the definition of "you", "yours", and "Barr", and to those Interrogatories that incorporate these terms, to the extent that such terms are purported to include "all of Barr Pharmaceuticals, Inc.'s and Barr Laboratories, Inc.'s corporate parents, corporate predecessors and past or present subsidiaries, affiliates, divisions, departments, officers, directors, principals, agents and employees," or other non-parties to this case.

10. Barr objects to the definition of "Document" and to those Interrogatories that incorporate the term to the extent that Plaintiffs' definition of such term differs from the meaning or exceeds the scope of the usage of the term in Federal Rule of Civil Procedure 34(a).

11. Barr objects to the definition of "the '318 patent" and to those Interrogatories that incorporate the term to the extent that such term is purported to include "any foreign counterpart" to U.S. Patent No. 4,663,318 or any patents other than the patent asserted by Plaintiffs in the Complaint (*i e* , U.S. Patent No. 4,663,318).

12. Barr objects to the numbering of the Interrogatories to the extent that particular interrogatories include discrete subparts that are not separately numbered. To the extent that the total number of interrogatories, including discrete subparts, exceeds the permitted number set forth in the Federal Rules of Civil Procedure, Barr reserves the right to refuse to answer all Interrogatories in excess of that number should the parties be unable to come to an agreement on the issue.

BARR'S SPECIFIC OBJECTIONS AND RESPONSE

INTERROGATORY NO. 2:

Separately for each claim, if you contend that any claim of the '318 patent is invalid for failure to comply with one or more of the provisions for patentability found in the U.S. Code, describe the basis for that contention.

RESPONSE:

Barr objects to this Interrogatory to the extent it seeks information relating to any claims other than claims 1 and 4 of the '318 patent, in light of the December 2, 2005 Stipulation Not to Contest Infringement. (*See* 12/2/2005 Stipulation, ¶ 4.) Barr objects to this Interrogatory to the extent this contention interrogatory is premature and may call for expert testimony. *See, e.g.*, Fed. R. Civ. P. 26(a)(2)(C). Barr objects to this Interrogatory as improperly being characterized as one interrogatory because its multiple subparts constitute separate interrogatories toward the presumptive 25 interrogatory limit. *See* Fed. R. Civ. P. 33(a). Barr notes that the Court has not yet construed any claim terms, phrases, or clauses of the asserted claims nor have Plaintiffs provided Barr with Plaintiffs' contentions as to the proper construction of any disputed claim terms, phrases, or clauses. Claim construction, which is an issue for the Court, is the first step in an infringement and/or invalidity analysis. Barr reserves the right to supplement this response on this basis and on the basis of any additional discovery consistent with the Federal Rules of Civil Procedure, the Local Rules of Civil Practice and Procedure of the United States District Court for the District of Delaware, and any relevant Orders of the Court. Barr further reserves the right to supplement its response to the extent that Plaintiffs change or otherwise supplement their contentions.

Subject to its general and specific objections, Barr responds to this Interrogatory as follows: Claim 1 of the '318 patent is directed to a "method of treating Alzheimer's disease and related dementias which comprises administering to a patient suffering from such a disease a therapeutically effective amount of galanthamine or a pharmaceutically-acceptable acid addition salt thereof." ('318 patent, claim 1.) Claim 1 is invalid under 35 U.S.C. § 102(b) as anticipated by at least P.A. Bhasker, *Medical Management of Dementia*, THE ANTISEPTIC, 71(1): 45-47 (1974) ("the Bhasker Article"). The Bhasker Article teaches treating "irreversible," "progressive

dementia," characterized by "a progressive fall-out of neurons and the course of the illness is rapidly downhill," with "small daily doses" of "Gallanthamine." One of ordinary skill in the art at the time of the invention would have understood the type of dementia described in the Bhasker Article to be or include at least Alzheimer's disease and/or related dementias. *See, e.g.*, K.L. Rathmann *et al.*, *Alzheimer's Disease: Clinical Features, Pathogenesis, and Treatment*, DRUG INTELL. CLIN. PHARM., 18: 684-91 (1984) ("the Rathmann Article") (teaches at least that Alzheimer's disease is a type of dementia); MERCK MANUAL (14th ed. 1982) (SYN RAZ 0006579-0006582) (teaches at least that Alzheimer's disease is a type of dementia "with a large loss of cells from the cerebral cortex and other brain areas," and that Alzheimer's dementia "progresses steadily."). One of ordinary skill in the art at the time of the invention would also have understood the Bhasker Article's "small daily doses" to be or include a "therapeutically effective amount." To the extent Plaintiffs contend any limitation of claim 1 of the '318 patent is not satisfied (and Plaintiffs have not to date), the claimed subject matter would have been obvious to one of ordinary skill in the art at the time of the invention in light of the Bhasker article alone, or in light of prior art articles or knowledge in the field as described further below.

Claim 4 of the '318 patent includes all of the limitations of claim 1 and further includes the limitations of "oral administration" in the range of "10–2000 mg per day." ('318 patent, claim 4.) Dosages within this range are a matter of routine experimentation and oral administration of galantamine[1] was well known. For example, claim 4 of the '318 patent is invalid as obvious, under 35 U.S.C. § 103 in view of the combination of the Bhasker Article and at least one of: D. Daskalov *et al.*, *Nivalin Application and Rehabilitation Treatment of Cerebral Diseases with Aphasic Syndromes*, MBI MEDICO-BIOLOGIC INFORMATION, 3: 9-11

(1980) ("the Daskalov Article") (teaches at least oral administration of daily dosages of galantamine to humans in dosages including 10 mg, 15 mg, and 20 mg daily); and the Rathmann Article (teaches at least oral administration of daily doses of acetylcholinesterase inhibitors—a class of drugs including galantamine—to humans for treatment of Alzheimer's disease, and specifically administration of the acetylcholinesterase inhibitor physostigmine in dosages including 12–15 mg daily). The Bhasker article alone or in combination with at least one of the Daskalov Article and the Rathmann Article renders claim 4 invalid as obvious under 35 U.S.C. § 103 because one of ordinary skill in the art would have required only routine experimentation to determine dosages within the range of "10-2000 mg per day" of galantamine of claim 4, particularly in light of the extensive knowledge about galantamine's use in humans. In addition, it would have been obvious to one of ordinary skill in the art at the time of the invention to orally administer galantamine, as required by claim 4, and shown by the Daskalov Article.

Claims 1 and 4 of the '318 patent are also invalid as obvious under 35 U.S.C. § 103 in view of the combination of any two or more of: R.C. Mohs *et al.*, *Intravenous and Oral Physostigmine in Alzheimer's Disease*, INTERDISCIPL. TOPICS GERONT., 20: 150-152 (1985) (teaches at least administration of oral dosages of acetylcholinesterase inhibitors—specifically physostigmine—to humans for treatment of Alzheimer's disease in dosages including 12–24 mg per day); K.G. Pernov, *Nivalin and its Curative Effect upon Diseases of the Nervous System*, PSYCHIATRY AND NEUROLOGY AND MEDICAL PSYCHOLOGY BULLETIN ON RESEARCH AND PRACTICE, 13(11): 416-20 (1961) (teaches at least that galantamine hydrobromide and physostigmine—both acetylcholinesterase inhibitors—are chemically similar (*i.e.*, both are tertiary amines)); D.A. Cozanitis, *L'hydrobromide de Galanthamine Unsubstitut du Sulfate*

[1] The terms galantamine and galanthamine are used interchangeably in the art.

D'eserine (Physostigmine) pour le Traitement des Effets Cerebraux des Substances Anti-Cholinergiques, NOUV. PRESSE MED., 7(45): 4152 (1978) (teaches at least that "galantamine hydrobromide . . . can have certain advantages over [physostigmine], due to its prolonged action," and that galantamine hydrobromide is able to cross the blood-brain barrier); UK Patent No. 942,200 (published 1963) (teaches at least that galantamine hydrobromide is "a strong anticholinesterase substance having an activity similar to that of [physostigmine], but showing a much less toxicity and a larger therapeutic range," and that galantamine hydrobromide acts on the central nervous system); B.S. Greenwald *et al*, *Experimental Pharmacology of Alzheimer's Disease*, THE DEMENTIAS, 87-102 (teaches at least that "[i]n every study in which multiple doses of a cholinomimetic agent have been administered to patients with AD, a positive effect of the drug has been noted," and that physostigmine's "relatively short duration of action renders it less desirable therapeutically in the long-term treatment on nonfluctuating clinical conditions, such as [Alzheimer's disease]") the Daskalov Article (teaches at least oral administration of daily dosages of galantamine to humans in dosages including 10 mg, 15 mg, and 20 mg daily); and the Rathmann Article (teaches at least oral administration of daily doses of acetylcholinesterase inhibitors—a class of drugs including galantamine—to humans in for the treatment of Alzheimer's disease, and specifically administration of the acetylcholinesterase inhibitor physostigmine in dosages including 12–15 mg daily).

Regarding claim 1 of the '318 patent, these prior art articles teach the use of acetylcholinesterase inhibitors—a class of drugs that includes physostigmine and galantamine—and physostigmine specifically, to treat Alzheimer's disease; that physostigmine has some drawbacks for treatment of Alzheimer's disease, including a relatively short duration of action; that galantamine hydrobromide and physostigmine are chemically similar (*i.e*, both are tertiary amines); that galantamine hydrobromide is a strong anticholinesterase substance having an

activity similar to that of physostigmine and can have certain advantages over physostigmine, including prolonged action, less toxicity, and a larger therapeutic range; and that galantamine, like physostigmine, was known to cross the blood-brain barrier. Consequently, it would have been obvious to one of ordinary skill in the art at the time of the invention to use galantamine to treat Alzheimer's disease and related dementias.

With respect to claim 4 of the '318 patent, these prior art articles additionally teach oral administration of both physostigmine and galantamine, and oral dosage ranges for both physostigmine and galantamine that fall within the claimed range of "10–2000 mg per day." Therefore, the claimed range of "10–2000 mg per day" of galantamine would have been obvious to one of ordinary skill in the art at the time of the invention. Additionally and/or alternatively, claim 4 is invalid as obvious under 35 U.S.C. § 103 because one of ordinary skill in the art at the time of the invention would have required only routine experimentation to determine dosages within the range of "10-2000 mg per day" of galantamine, as required by claim 4. Additionally, it is taught in the prior art and it would have been obvious to one of ordinary skill in the art at the time of the invention to orally administer galantamine, as required by claim 4.

Other prior art provides further support for Barr's contention that the '318 patent is invalid as being either anticipated under 35 U.S.C. § 102 (art reflecting knowledge in the field) or obvious under 35 U.S.C. § 103, including: A.R. Luria *et al*, *Restoration of Higher Cortical Function Following Local Brain Damage*, DISORDERS OF HIGHER NERVOUS ACTIVITY, Ch. 21 (P.J. Vinken and G.W. Bruyn ed., North Holland Publishing Company 1969); B.S. Greenwald *et al*, *Neurotransmitter Deficits in Alzheimer's Disease: Criteria for Significance*, J. AM. GERIATRICS SOC'Y, 31: 310-16 (1983); D.A. Cozanitis, *Galanthamine Hydrobromide, a Longer Acting Anticholinesterase Drug, in the Treatment of Central Effects of Scolpamine (Hyoscine)*, ANAESTHESIST, 26:649-50 (1977); L.J. Thal *et al*, *Oral Physostigmine and Lecithin Improve*

Memory in Alzheimer Disease, ANNALS OF NEUROLOGY, 13:491-96 (1983); L.N. Nesterenko, *Influence Exerted by Galantamine on the Acetylcholinesterase Activity*, FARMAKOL TOKSIKOL, 28: 413-14 (1965); W. Göpel *et al.*, *Erfahrungen mit Nivalin in der Neurologischen Therapie*, PSYCHIAT. NEUROL. MED. PSYCHOL., 23: 712-18, (1971); C.M. Smith *et al.*, *Physostigmine in Alzheimer's Disease*, THE LANCET, 1: 42 (1979); R.C. Mohs *et al.*, *Clinical Studies of the Cholinergic Deficit in Alzheimer's Disease*, J. OF THE AM. GERIATRICS SOC'Y, 33(11): 749-57 (1985); R.C. Mohs *et al*, *Oral Physostigmine Treatment of Patients With Alzheimer's Disease*, AM. J. OF PSYCHIATRY, 142(1): 28-33 (1985); V. Haroutunian *et al.*, *Cholinergic Modulation of Memory in Rats*, PSYCHOPHARMACOLOGY, 87(3): 266-71 (1985); K.L. Davis *et al.*, *Oral Physostigmine in Alzheimer's Disease*, PSYCHOPHARMACOLOGY BULLETIN, 19(3): 451-53 (1983); M.I. Levy *et al.*, *Research Subject Recruitment for Gerontological Studies of Pharmacological Agents*, NEUROBIOLOGY OF AGING, 3(1): 77-79 (1982); R. Yu. Il'yutchenok *et al.*, *Cholinergic Mechanisms of Memory. Analysis of the Amnesic Effect of Anticholinergic Drugs*, INT'L J. OF PSYCHOBIOLOGY, 2(3): 177-92 (1972); R. Yu. Il'yutchenok, *Pharmacological Aspects of Memory Neurochemical Regulation*, BULGARIAN ACADEMY OF SCIENCES: ACTA PHYSIOLOGICA ET PHARMACOLOGICA BULGARICA, 8(1-2): 43-49 (1982); V.A. Krauz *et al.*, *Role of Cholinergic Mechanisms in ATFase Activity and Glycolysis Intensity Regulation in the Rat Neocortex, Hippocampus and Truncus Cerebri*, FARMAKOLOGIA I TOKSIKOLOGIA, 1: 23-26 (1982); A. Plaitakis *et al*, *Homer's Moly Identified As Galanthus Nivalis L.: Physiologic Antidote to Stramonium Poisoning*, CLINICAL NEUROPHARMACOLOGY, 6(1): 1-5 (1983); M. Bretagne *et al*, *Essais Cliniques en Anesthesiologie D'un Nouvel Anticholinesterasique la Galanthamine*, ANESTHESIE ANALGESIE REANIMATION, 1: 285-92 (1965); G. Milbled *et al*, *Sur L'action Centrale de la Galanthamine*, COMPETES RENDUS DES SEANCES DE LA SOCIETE DE BIOLOGIE ET DE SES FILIALES, 160(11): 2089-90 (1966); R. Yu. Il'yuchenok *et al*, *Comparison*

of the Effects Produced By Anticholinergic and Anticholinesterase Substances on Induced Potential of the Cerebral Cortex, FARMAKOLOGIA I TOKSIKOLOGIA, Vol. 1 (1969); R. Yu. Il'yutchenok, *Cholinergic Brain Mechanisms and Behaviour*, PROGRESS IN BRAIN RESEARCH: ANTICHOLINERGIC DRUGS AND BRAIN FUNCTIONS IN ANIMALS AND MAN, 28: 134-48 (1968); D.A. Cozanitis *et al.*, *A Comparative Study of Galanthamine Hydrobromide and Atropine/Neostigmine in Conscious Volunteers*, THE ANAESTHESIST, 416-21 (1971); K.L. Davis *et al.*, *Physostigmine: Improvement of Long-Term Memory Processes in Normal Humans*, SCIENCE, 201(4352): 272-74 (1978); K.L. Davis *et al.*, *Enhancement of Memory Processes in Alzheimer's Disease with Multiple-Dose Intravenous Physostigmine*, THE AM. J. OF PSYCHIATRY, 139(11): 1421-24 (1982); B.H. Peters *et al.*, *Effects of Physostigmine and Lecithin on Memory in Alzheimer Disease*, ANNALS OF NEUROLOGY, 6(3): 219-21 (1979); and Von K.G. Pernov, *Das Nivalin und seine Heilwirkung bei Erkrankungen des Nervensystems*, PSYCHIATRIE NEUROLOGIE UND MEDIZINISCHE PSYCHOLOGIE, 13(11): 416-20 (1961). Barr further reserves its right to rely upon any additional prior art identified by Plaintiffs, Barr, and/or any other Defendant against whom the '318 patent is asserted.

With respect to the issue of obviousness, Plaintiffs have to date identified no evidence in support of any secondary considerations of non-obviousness that affect the obviousness of the claims.

To the extent Plaintiffs contend that claims 1 and/or 4 are not anticipated or rendered obvious by the prior art, the claims are invalid for failure to satisfy the enablement requirement under 35 U.S.C. § 112, ¶ 1. "[T]o satisfy the enablement requirement of section 112, an applicant must describe the manner of making and using the invention 'in such full, clear, concise and exact terms as to enable any person skilled in the art . . . to make and use the same . . . .'" *See Rasmusson v. SmithKline Beecham Corp*, 413 F.3d 1318, 1322 (Fed. Cir. 2005)

(quoting 35 U.S.C. § 112, ¶ 1). In the case of determining the utility of a drug or medicament, to enable an invention, an inventor has to do more than "merely propos[e] an unproved hypothesis." *Id.* at 1325. Mere plausibility is not enough. *See Id.* "If mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to 'inventions' consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the 'inventor' would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis." *Id.* The '318 patent identifies no tests or studies in support of the claimed method of use, identifies no unknown property of the drug galantamine, and identifies no unknown scientific principle related to Alzheimer's or the effect of galantamine in the human body. "[W]here there is 'no indication that one skilled in the art would accept without question statements as to the effects of the claimed drug products and no evidence has been presented to demonstrate that the claimed products do have those effects,' an applicant has failed to demonstrate sufficient utility and therefore cannot establish enablement." *Id.* at 1323.

To the extent Plaintiffs contend Dr. Bonnie Davis invented anything not already known in the field, and therefore not anticipated under Section 102(b) nor obvious under Section 103, the '318 patent fails to provide an enabling disclosure and written description within the meaning of Section 112.

In addition, claim 4 is further invalid under 35 U.S.C. § 112, ¶ 1 because the inventor failed to teach one of ordinary skill in the art how to make or use the invention over the full scope of the recited range. Specifically, the specification does not teach one of ordinary skill that the entire recited range of "10-2000 mg per day" is a "therapeutically effective amount" as

required by claim 1. Therefore, claim 4 fails to provide both an enabling disclosure and an adequate written description under 35 U.S.C. § 112.

Respectfully submitted,

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Dated: April 13, 2006

CERTIFICATE OF SERVICE

The undersigned attorney certifies that he caused two copies of the foregoing Defendants Barr Pharmaceuticals, Inc.'s and Barr Laboratories, Inc.'s Supplemental Objections and Response To Plaintiffs' Interrogatory No. 2 to be served by hand on the 13th day of April, 2006 upon:

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